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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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NEKTAR THERAPEUTICS
150 INDUSTRIAL ROAD
SAN CARLOS, CA 94070

EXAMINER	
MONDESI, ROBERT B	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 06/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/789,956	BOSSARD ET AL.	
	Examiner	Art Unit	
	Robert B. Mondesi	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-61* is/are pending in the application.

4a) Of the above claim(s) *31-61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the amendment filed March 28, 2005. **Claims 1-30** as drawn to elected Invention I are currently pending and are under examination.

Withdrawal of Objections and Rejections

The objection to the specification on the basis of incorrect use of Trademarks is withdrawn.

Maintenance of rejections

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

Claims 14 remains rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim Rejections - 35 USC § 102

Claims 1-7, 12-15, 17-22, 24 and 26-30 remain rejected under 35 U.S.C. 102(b) as being anticipated by Minamino et al. United States Patent 6,037,452 (cited in the IDS filed October 28, 2004).

Claim Rejections - 35 USC § 103

Claims 1, 3-4 and 8-10 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Minamino et al. in view of Davis et al. (cited in the IDS filed November 15, 2004).

Claims 1, 3-4 and 8-11 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Minamino et al. in view of Greenwald (cited in The IDS filed November 15, 2004).

Claims 1,14 and 16 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Rostin et al. in view of Greenwald.

Claims 1, 23 and 25 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Minamino et al. in view of Longenecker et al. United Stated Patent 4,994,439.

The above rejections were explained in the previous Office action.

Response to applicants' arguments

In regards to the rejection of **Claim 14** under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, the applicants assert that the term biologically active fragments is no longer recited in the claim 14, therefore the claim has been rendered moot.

Applicants' argument has not been found persuasive because the following phrases still remain in the claim: "deletion variants, substitution variants or addition variants of any of the forgoing", as indicated previously in the Office action mailed

December 23, 2004 the applicants have not provided a written description for the mentioned variants.

In regards to the rejection of **claims 1-7, 12-15, 17-22, 24 and 26-30** under 35 U.S.C. 102(b) as being anticipated by Minamino et al., the applicants assert that each of the claims requires a composition comprising a plurality of conjugates, wherein at least about 82% of conjugates in the composition each has one to three water soluble polymers covalently attached to a Factor VIII moiety, whereas Minamino et al. teach Factor VIII conjugates "containing polyalkylene glycol added to about 50-70% of amino groups in molecules." Applicants assert further that in native Factor VIII, there are "158 amine-containing lysine residues (6.8 weight percent of the entire protein) ", thus Minamino et al. effectively teach only Factor VIII conjugates comprising about 79-110 (50-70% of 158) polyalkylene glycol polymers attached to Factor VIII and therefore the reference does not teach the claimed element of the composition.

Applicants' arguments have not been found persuasive. First and foremost the examiner would like to address the relative term "at least about", nowhere in the specification have the applicants stated the lower or upper limit of the relative term "about"; therefore it is reasonable to assume that 70% would be close enough to 82% in order to fall within the range of about 82%; however, with regards to "at least about" the court held that claims reciting "at least about" were invalid for indefiniteness where there was close prior art and there was nothing in the specification, prosecution history, or the prior art to provide any indication as to what range of specific activity is covered by the

term "about." Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d1200, 18 USPQ2d 1016 (Fed. Cir. 1991).

Secondly, it must be noted that nowhere in the specification have the applicants' themselves disclosed a composition comprising a plurality of conjugates, wherein at east about 82% of conjugates in the composition each has one to three water soluble polymers covalently attached to a **native** Factor VIII moiety, the example that the applicants have pointed to, in order to provide support for their amendment only addresses B-domain deleted Factor VIII and not native Factor VIII in such case the applicants' calculations with regards to 82% conjugated Factor VIII is incorrect, as the undoubtedly the applicants are well aware that B-domain deleted Factor VIII will not have the same number of amine-containing lysine residues as the native Factor VIII (for more in regards to support for amended **claim 1** please refer to the written description rejection of **claims 1-15 and 17-30** in the new rejections section of this Office action).

Thirdly, Minamino et al. do not state that their composition only comprises PEG conjugated Factor VIII in the range of 50-70 %, but rather state that the percentage of the PEG added to the modified Factor VIII can be measured by determining the unaltered amino groups with trinitobenzene sulfonic acid, and those containing PEG added to about 50-70% of amino groups in molecules **may be structurally useful.**

Minamino et el. teach further that the molar ratio between the peptide and the polyalkylene glycol can be regulated to control the degree of substitution of the peptide chain, bearing in mind the length of the peptide chain under consideration and

modification degrees of specific amino acids (where specific amino acids are known to be reacted with specific coupling agents such as reaction of .epsilon.-amino groups of lysine with sodium 2,4,6-trinitrobenzene sulfonate) can be determined based on concentration of the coupling agent or modified poly(alkylene oxide) and pH employed in the reaction with the peptide. Various combinations of high pH (about 6.5 to 10) or low pH (about 3.0 to 6.0) with high or low concentration (1.0 to 4.0 molar or 0.1 to 1.0 molar) can provide various degrees of substitution, all of which is quantitatively measured in accordance with conventional analytical techniques, such as mentioned above (Column 7, lines 65-68 and Column 8, lines 1-5).

In regards to the rejection of **claims 1, 3-4 and 8-10** under 35 U.S.C. 103(a) as being unpatentable over Minamino et al. in view of Davis et al., **claims 1, 3-4 and 8-11** under 35 U.S.C. 103(a) as being unpatentable over Minamino et al. in view of Greenwald **claims 1,14 and 16** remain rejected under 35 U.S.C. 103(a) as being unpatentable over Rostin et al. in view of Greenwald, **claims 1, 23 and 25** under 35 U.S.C. 103(a) as being unpatentable over Minamino et al. in view of Longenecker et al., the applicants assert that the three criteria for establishing a *prima facie* case of obviousness has not been established because when the prior art references do not teach or suggest or describe conjugate containing compositions wherein at least about 82% of conjugates in the composition each has one to three soluble polymers covalently attached to a Factor VIII moiety.

Applicants' arguments have not been found persuasive for the reasons mentioned above, as the new limitations of **claim 1** have been addressed in view of the primary reference, Minamino et al.

New rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15 and 17-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

On page 11 of the response filed March 28, 2005, the applicants state that **claim 1** has been amended to recite conjugate-comprising compositions "wherein at least about 82% of the conjugates in the composition each has one to three water-soluble polymers covalently attached to a Factor VIII moiety and support for the change can be found in the Experimental, where for example, at least about 82% (~39% + ~32% + ~11%) of the conjugates in the composition described in Example 6 each has one to three water polymers attached to Factor VIII moiety.

The examples in the specification that the applicants have cited only provide support for B-domain deleted conjugated Factor VIII whereas **claim 1** reads on a variety of Factor VIII polypeptides including but not limited to native Factor VIII, Factor VIIIa, Factor VIII:C and Factor VIII:vWF. In fact, nowhere in the specification have the applicants described a composition comprising a plurality of conjugates, wherein at least about 82% of conjugates in the composition each has one to three water soluble polymers covalently attached to **native** Factor VIII moiety.

Claims 1-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In **claim 1** the applicants use the phrase "at least about" 82% of conjugates ..., the court has held that claims reciting **"at least about"** were invalid for indefiniteness where there was close prior art and there was nothing in the specification, prosecution history, or the prior art to provide any indication as to what range of specific activity is covered by the term "about." Amgen, Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991). **Claims 2-30** are included because they are dependet claims that do not further clarify the independent claim for which they depend.

Conclusion

No claims are allowed.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert B Mondesi whose telephone number is 571-272-0956. The examiner can normally be reached on 9am-5pm, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert B. Mondesi
Patent Examiner
Group 1653
06-10-05

ROBERT A. WAX
PRIMARY EXAMINER
Art Unit 1653